

REMARKS

Claims 19 and 27-30 have been canceled.

Claim 1 has been amended.

This Amendment adds no new matter.

Additional remarks are set forth below with reference to the rejections set forth in the Office Action.

Paragraph 7. Rejection of Claims 1-30 Under 35 U.S.C. § 103(a)

Claims 1-3 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 5,210,098 to Nath in view of DiPiro, Editor-in-Chief, Pharmacotherapy, A Pathophysiologic Approach, pp 515-24, 1989 in view of Solomons, T.W., Organic Chemistry, Third Edition, pp 794-7, 814-5, 1984.

The Examiner asserts that Nath teaches that a pyruvate salt, such as sodium pyruvate, may be utilized in the treatment of acute renal failure (Office Action, Page 3). The Examiner further states that Nath teaches that it is known in the art that alpha-keto acids may be utilized to affect the progression of established renal disease and that pyruvate and other alpha-keto acids exert cytoprotection against peroxide-induced oxidant stress (Office Action, Page 3). The Examiner also states that DiPiro teaches that acute renal failure has several different etiologies (Office Action, Page 3). The Examiner asserts that it would have been obvious to one having ordinary skill in the art to identify risk factors of acute renal failure and treat and prevent the development of additional complications and to combine various pharmaceutical agents to treat the symptoms of acute renal failure (Office Action, Page 4). According to the Examiner, the difference between Nath and DiPiro and the present application is that Nath teaches an alpha-keto acid or salt of an alpha keto acid whereas the present claims are directed to the use of an alpha-keto acid ester (Office Action, Page 4). Solomons is relied on for the teaching that a carboxylic acid ester can be prepared by reacting a carboxylic acid moiety with an alcohol (Office Action, Page 4). The Examiner is of the opinion that the skilled artisan would have been motivated by the teachings of Nath to use an alpha-keto acid, such as pyruvate, to prepare an ester and utilize the ester to treat acute renal failure (Office Action, Pages 4-5). Where the

claimed invention is rejected as *prima facie* obvious in view of a combination of references, M.P.E.P. § 2142 requires that "there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings." M.P.E.P. § 2142 further provides that "[t]he teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

The combined teachings of Nath, DiPiro and Solomons do not provide the suggestion or motivation to treat acute renal failure with an ester of pyruvate. Nath teaches the use of pyruvate salts for the treatment of acute renal failure:

The present invention provides a therapeutic method comprising administration of an amount of a pyruvate salt to a patient experiencing, or in danger of, acute renal failure. The pyruvate salt, preferably sodium pyruvate, is preferably dispersed or dissolved in a pharmaceutically acceptable liquid carrier and administered parenterally in an amount effective to arrest or prevent said acute renal failure, thus permitting restoration of normal kidney function.

(column 2, lines 13-21) (emphasis added). Nath's teachings are limited to the use of pyruvate salts, such as sodium pyruvate and other salts:

Although the invention has been exemplified by reference to sodium pyruvate, other nontoxic alkali metal, alkaline earth metal, ammonium and substituted amine salts of pyruvic acid can also be employed.

(column 6, lines 57-60). Nath does not teach or suggest using a pyruvate ester or indeed any 2-ketoalkanoic acid ester to treat acute renal failure. The teachings of Nath would, therefore, not have provided one having ordinary skill with the motivation to treat acute renal failure with a pyruvate ester.

DiPiro and Solomons do not add to the teachings of Nath to support a *prima facie* obviousness rejection. DiPiro describes the symptoms and etiology of acute renal failure. Although DiPiro teaches that agents such as mannitol, furosemide and dopamine have been used in the treatment of acute renal failure (page 520), DiPiro does not teach that a 2-ketoalkanoic acid ester can be used to treat acute renal failure.

Solomons, in a section entitled, "Synthesis of Esters: Esterification," teaches various methods for the synthesis of carboxylic acid esters. Solomons, however, does not teach any method for the treatment of acute renal failure. Solomons is directed exclusively to the chemical synthesis of esters and provides no teachings as to the treatment of any disease or condition. Therefore, neither DiPiro nor Solomons provide any suggestion of the use of a pyruvate ester in the treatment of acute renal failure. Furthermore, neither of Nath, DiPiro or Solomons alone or in combination teaches or suggests that administration of a pyruvate ester would be advantageous or effective in the treatment of acute renal failure. In the absence of any teaching that a pyruvate ester would be beneficial or even effective in treating acute renal failure, one of ordinary skill would have had no motivation to substitute the pyruvate salt taught by Nath with a pyruvate ester of the present claims. Therefore, the claimed invention is non-obvious over the combined teachings of Nath, DiPiro and Solomons.

Accordingly, given that the combined teachings of Nath, DiPiro and Solomons do not provide the requisite suggestion or motivation to establish *prima facie* obviousness, reconsideration and withdrawal of the rejection is respectfully requested.

Respectfully submitted,

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